

S. O. [Signature]
8/23/91

PATENT



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: : Allowed: June 28, 1991 *H 27/Ryan*
MOHIUDDIN ET AL. : Issue Fee Due:
Serial No. 07/330,156 : September 30, 1991
Filed March 29, 1989 :
For: NOVEL METHOD OF : Batch No. Q89
MYOCARDIAL IMAGING : Group Art Unit: 336
: Examiner: M. POLUTTA
: Attorney Docket No.:
7253-004

RESPONSE BY APPLICANTS
TO THE PROTEST
FILED UNDER 37 C.F.R. §1.291(a)

Honorable Commissioner of Patents and Trademarks,
Washington, D.C. 20231

Sir:

This is in response to the Protest Under 37 C.F.R. § 1.291(a) filed on July 12, 1991 by John W. Ryan (Reg. No. 33,771) ("Protestor") of White & Case, 1155 Avenue of the Americas, New York, New York 10036, for the above identified application.

The Protestor has cited the reference, Sollevi, A., "Cardiovascular Effects of Adenosine in Man; Possible Clinical Implications", Progress in Neurobiology, Vol. 27, pp. 319-349 (1986) ("Sollevi"). The Protestor alleges this reference is relevant to the subject application because of its discussion of the cardiovascular effects of adenosine in man. The Protestor has also pointed to table 6 of this reference and alleges that this table discloses adenosine is useful as a preferential myocardial vasodilator, and may have some tentative use in "diagnosticum".

Applicants respectfully submit that the Sollevi reference is not material with regard to the novel methods claimed in the present application. In addition, the subject matter described in Sollevi has already been thoroughly discussed with the Examiner and the Examiner has allowed the pending claims and issued a Notice of Allowance for the present application in view of this information. Furthermore, under 37 C.F.R. §1.291(a) and MPEP §1901.04 this Protest is untimely since it was filed after a Notice of Allowance was issued and the reference cited is not material.

Sollevi is simply a review article concerning the effects of adenosine in man. It also presents some alleged possible future clinical implications of adenosine administration. The reference discusses ways to detect adenosine levels in different body tissue and the effects of administering adenosine to humans. The reference also discusses that adenosine is a vasodilator and can be used, for example, to induce controlled hypotension and increase myocardial blood flow. The reference also proposes that adenosine can be used as a vasodilator to counteract vasospasms that occur after subarachnoid hemorrhage or vasospasms that occur during angioplasty of coronary artery stenosis. In Table 6 of the Sollevi reference it is also tentatively proposed that adenosine can be used in "diagnosticum." In conclusion, Sollevi alleges that adenosine may be used in many clinical situations as a vasodilator, antiaggregatory compound as well as an antiarrhythmic agent. The author also gives various dosage ranges of adenosine and states that "both the physiological

and pharmacological aspect of adenosine are subject to intense study in several laboratories."

Applicants respectfully submit that the Sollevi reference is not material in relation to the novel methods claimed in the present application and it raises no issues which were not already before the Examiner. Applicants have already extensively discussed through amendments and interviews with the Examiner, the various uses of adenosine. In particular, applicants have disclosed that adenosine can be used in humans as a vasodilator and that it has various other uses such as causing hypotension, and is useful as an antiarrhythmic agent.¹ Most importantly, in the Information Disclosure Statement filed on February 11, 1991 for the present application, applicants cited PCT Publication No. WO 87/01593 wherein one of the named inventors is Alf Sollevi, the author of the reference cited by the Protestor. This PCT application contains the same general information found in the Sollevi reference, i.e., the use of adenosine for the induction of controlled hypotension, control of hypertensive crisis, effective preferential coronary vasodilation, increasing blood flow in a coronary artery graft, increasing cardiac output, reducing platelet loss during coronary bypass surgery and facilitation of the induction of cardioplegia. The Sollevi PCT published application discloses nothing about the use of adenosine in diagnosis or detecting the presence and assessing the severity of

¹ See, for example, Biaggioni et al., and Berne et al. which were cited to the U.S. Patent Office in Information Disclosure Statements filed on February 11, 1991 and March 26, 1991 respectively. In addition, these references, as well as others, are discussed in the amendments filed on February 27, 1991 and June 3, 1991 for the present application.

myocardial dysfunction. Clearly, the Sollevi reference was only speculation as to some possible future clinical uses of adenosine since when Sollevi filed his PCT application he did not include any disclosure related to diagnosis using adenosine.

None of these above described uses of adenosine disclosed in the Sollevi reference and the Sollevi published PCT application have any relation to the novel methods claimed in the present application, which involve detecting the presence and assessing the severity of myocardial dysfunction in a human by administering to said human an adenosine receptor agonist and performing a technique on said human to detect the presence and assess the severity of myocardial dysfunction. In particular, the myocardial dysfunction being detected by using the novel methods of the present invention include coronary artery disease, ventricular dysfunction and differences in blood flow through disease free coronary vessels as opposed to stenotic coronary vessels. The uses of adenosine discussed in the Sollevi reference and PCT application make no mention of using adenosine in humans in these novel methods. In addition, the mere use of the word "diagnosticum" in Table 6 on page 345 of the Sollevi reference does not describe or make obvious the novel methods of the present invention. In conclusion, a person skilled in the art, having the Sollevi reference in hand, would not be led to the novel methods claimed in the present application.

Thus, since applicants have already disclosed and discussed any issues raised by the Sollevi reference and shown that they are not material in relation to the novel methods claimed in the present application, this reference

should not affect the claims allowed and the Notice of Allowance which has already been issued by the Examiner.

Furthermore, under 37 C.F.R. §1.291(a) any protest filed by a member of the public against a pending application must be filed "timely." MPEP §1901.04 states in order for a protest to be considered timely, it must be filed before final rejection or before allowance of the application. While the Examiner is given discretion to consider a protest filed after a Notice of Allowance has been issued, this discretion should only be exercised by the Examiner if the protest raises serious new issues.

This protest was filed after a Notice of Allowance had been issued by the Examiner for the present application. Furthermore, as applicants have discussed supra, the Sollevi reference raises no new issues which were not already discussed with the Examiner. In addition, the Sollevi reference discloses similar information as found in the Sollevi PCT published application which was cited to the U.S. Patent Office by applicants and distinguished from the novel methods claimed in the present application.

In conclusion, the Sollevi reference is not material to the novel methods claimed in the present application and should not effect the allowed claims. In addition, since Sollevi is not material to the examination of this application and the present protest was filed after a Notice of Allowance was issued by the Examiner, the Examiner should take no action with regard to the present protest and allow this application to issue to a patent.

If the Examiner has any questions concerning this response, the Examiner is respectfully invited to call the undersigned to discuss the matter further.

Respectfully submitted,

Date 7/23/91

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1991
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Mohuiddin et al. #27

Serial No.: 231,217

Group No.: 183

Filed: 8/11/88

Examiner:

For: USE OF ADENOSINE AND ITS DERIVATIVES IN DIAGNOSIS

Commissioner of Patents and Trademarks
Washington, D.C. 20231

PROTEST UNDER 37 CFR 1.291(a)

Sir:

This protest against the above-identified application is
made in view of the prior art reference:

Progress in Neurobiology Vol. 27, pp. 319-349 (1986). A
copy of this relevant publication is enclosed and is also
listed on an accompanying PTO 1449 form.

This reference is relevant to the subject application
because of its discussion of the cardiovascular effects of
adenosine in man. In particular, the disclosure in Table 6
of adenosine as a preferential coronary vasodilator and the

suggested utility as a diagnostic is relevant. See pages 344 and 345.

Service of a complete copy of these papers was made by depositing copies of these papers with the United States Postal Service on July 12, 1991 each with sufficient postage as first class mail in an envelope addressed to each of the following:

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Respectfully submitted,

DATE: July 12, 1991

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